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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/977,034 | 10/11/2001 | Kin-Ming Lo | LEX-009DV | 4315 |
| 21323 | 7590 | 01/29/2004 | EXAMINER | |
| TESTA, HURWITZ & THIBEAULT, LLP HIGH STREET TOWER 125 HIGH STREET BOSTON, MA 02110 | | | | JIANG, DONG |
| | | ART UNIT | | PAPER NUMBER |
| | | 1646 | | |

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-----------------|--------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/977,034 | LO ET AL. |
| | Examiner | Art Unit |
| | Dong Jiang | 1646 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 05 November 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 26-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 26-38 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) Interview Summary (PTO-413) Paper No(s) _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED OFFICE ACTION

Applicant's amendment filed on 05 November 2003 is acknowledged and entered. Following the amendment, claims 26, 27 and 38 are amended.

Currently, claims 26-38 are pending and under consideration.

Withdrawal of Objections and Rejections:

The rejection of claims 26-38 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

New Matter Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly amended claims 26, 27 and 38 recite "at least a portion of an IgG3 chain constant region". Applicants have not pointed out, nor can the Examiner locate, the basis in the specification for such a limitation.

This is a new matter rejection.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 28-30, 34-36 and 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, taken with Lo et al., US 5,541,087, for the reasons of record set forth in the last Office Action, paper No. 7, mailed on 05 May 2003, at pages 3-4.

Applicants argument filed on 05 November 2003 has been fully considered, but is not deemed persuasive for reasons below.

At page 6 of the response, the applicant argues that Chang teaches away from the claimed invention as Chang states that using the IgG4 as the Fc moiety is advantageous and preferred, and that the G4, unlike G1, avoids the wide spectrum of secondary biological properties such as complement fixation and ADCC. Applicants further argue that in contrast, the present invention uses a Fc region derived from at least a portion of an IgG1 or an IgG3 constant region. This argument is not persuasive for the following reasons. First, although IgG4 is preferred in Chang's teachings, IgG1 is not excluded. In fact, Chang's claims encompass Fc from IgG1, as only one claim (claim 4) is limited to the Fc of IgG4. There is no merit to the argument that the rejection must be over the preferred embodiment. Further, the art has established that when the Fc region of IgG4 is separated from the Fab region, the Fc of IgG4 fixes complement as well as the Fc region of IgG1 (Isenman, D. E. et al. (1975) J. IMMUNOL. 114: 1726, the abstract), indicating that there is no significant difference between IgG1 Fc and IgG4 Fc in this regard. Additionally, art has established the wide use of IgG1 Fc in fusion molecules, for example, the teachings by Lo, which is reviewed in the last Office Action. Briefly, Lo discloses a fusion protein expression system comprising, from its 5' to 3' direction, a signal sequence, an immunoglobulin Fc region, and target protein

Art Unit: 1646

sequence, and indicates that the system is generally useful for protein expression. Additionally, Lo teaches that if the fusion protein is to be used as a biopharmaceutical, the Fc domain may confer the effector function activities to the fusion protein, such as a longer serum half-life. Further, Lo teaches that the Fc γ 1 region includes at least a portion of the hinge domain, and CH3 domain, or at least a portion of the hinge domain, CH2 and CH3 domains. Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a fusion Fc-IFN- α protein, wherein the Fc region is derived from either IgG1 or IgG4 for treating a condition such as hepatitis, and would have expected success because Isenman has demonstrated that the Fc of IgG4 fixes complement as well as that of IgG1 when separated from the Fab.

At pages 6-7 of the response, the applicant argues that applicants have discovered a new and unobvious property of moderating effector functions upon binding to the IFN- α receptor by occluding the Fc residues that mediate ADCC and complement fixation (as taught in the specification at page 10, lines 12-15), wherein the Fc of the fusion protein is derived from at least a portion of an IgG1 or IgG3. Applicants further argue that the art failed to appreciated the advantage of using a fusion protein that benefits from this unexpected property. This argument is not persuasive for the following reasons. First, the specification, as applicants pointed out, merely teaches Fc-X in general, and it does not specify that only the Fc of IgG1 or IgG3 is associated with said advantage, and in fact, IgG3 is never mentioned in the specification, and is accordingly rejected as new matter. As such, and as the combined prior art teaches other advantages to make a Fc fusion protein comprising IFN- α for treating hepatitis, the present method of treatment is obvious over the prior art. Further, although none of the references mentions explicitly the effect by occluding the Fc residues, such an "unexpected property" would be inherent because the combined art teaches the same composition used for the same method for the same purpose. "By occluding the Fc residues" is at the most a newly discovered mechanism/result of a known process, and newly discovered mechanism of known processes directed to same purpose are inherent, and therefore, the instant claims are not patentable over the prior art.

Note: the newly cited reference is merely for the purpose of rebuttal, and it is not for sustaining any new ground rejection.

Claims 27, 31-33 and 37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., US 5,723,125, and Lo et al., US5,541,087, as applied to claims 26, 28-30, 34-36 and 38 above, and further in view of Capon et al., US5,116,964, for the reasons of record set forth in the last Office Action, paper No. 7, mailed on 05 May 2003, at pages 4-5.

Applicants argument filed on 05 November 2003 has been fully considered, but is not deemed persuasive for the same reasons above as the same argument for the above rejection is applied here.

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
1/21/04



LORRAINE SPECTOR
PRIMARY EXAMINER